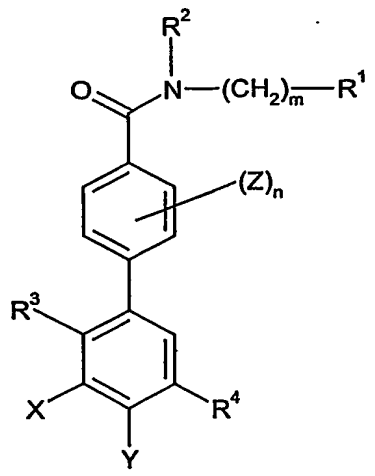
CLAIMS

1. A compound of formula (I):



(I)

wherein

R^1 is selected from hydrogen, C_{1-6}alkyl optionally substituted by up to three groups independently selected from C_{1-6}alkoxy, halogen and hydroxy, C_{2-6}alkenyl, C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, phenyl optionally substituted by up to three groups independently selected from R^5 and R^6, and heteroaryl optionally substituted by up to three groups independently selected from R^5 and R^6,

R^2 is selected from hydrogen, C_{1-6}alkyl and $-(CH_2)_p-C_{3-7}$cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups,

or $(CH_2)_mR^1$ and R^2, together with the nitrogen atom to which they are bound, form a four- to six-membered heterocyclic ring optionally substituted by up to three C_{1-6}alkyl groups;

R^3 is chloro or methyl;

R^4 is the group $-NH-CO-R^7$ or $-CO-NH-(CH_2)_p-R^8$;

R^5 is selected from C_{1-6}alkyl, C_{1-6}alkoxy, $-(CH_2)_p-C_{3-7}$cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, $-CONR^9R^{10}$, $-NHCOR^{10}$, $-SO_2NHR^9$, $-(CH_2)_qNHSO_2R^{10}$, halogen, CN, OH, $-(CH_2)_qNR^{11}R^{12}$, and trifluoromethyl;

R^6 is selected from C_{1-6}alkyl, C_{1-6}alkoxy, halogen, trifluoromethyl and $-(CH_2)_qNR^{11}R^{12}$;

R^7 is selected from hydrogen, C_{1-6}alkyl, $-(CH_2)_p-C_{3-7}$cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, trifluoromethyl, $-(CH_2)_r$heteroaryl optionally substituted by R^{13} and/or R^{14}, and $-(CH_2)_r$phenyl optionally substituted by R^{13} and/or R^{14};

R^8 is selected from hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, $CONHR^9$, phenyl optionally substituted by R^{13} and/or R^{14}, and heteroaryl optionally substituted by R^{13} and/or R^{14};

R^9 and R^{10} are each independently selected from hydrogen and C_{1-6}alkyl, or

R^9 and R^{10}, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15}, wherein the ring is optionally substituted by up to two C_{1-6}alkyl groups;

R^{11} is selected from hydrogen, C_{1-6}alkyl and -$(CH_2)_p$-C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups,

R^{12} is selected from hydrogen and C_{1-6}alkyl, or

R^{11} and R^{12}, together with the nitrogen atom to which they are bound, form a five or six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15};

R^{13} is selected from C_{1-6}alkyl, C_{1-6}alkoxy, –$(CH_2)_p$-C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, -$CONR^9R^{10}$, -$NHCOR^{10}$, halogen, CN, -$(CH_2)_qNR^{11}R^{12}$, trifluoromethyl, phenyl optionally substituted by one or more R^{14} groups and heteroaryl optionally substituted by one or more R^{14} groups;

R^{14} is selected from C_{1-6}alkyl, C_{1-6}alkoxy, halogen, trifluoromethyl and -$NR^{11}R^{12}$;

R^{15} is selected from hydrogen and methyl;

X and Y are each independently selected from hydrogen, methyl and halogen;

Z is selected from -$(CH_2)_sOR^{16}$, -$(CH_2)_sNR^{16}R^{17}$, -$(CH_2)_sCH_2CH_2R^{16}$, -$(CH_2)_sCOOR^{16}$, -$(CH_2)_sCONR^{16}R^{17}$, -$(CH_2)_sNHCOR^{16}$, -$(CH_2)_sNHCONR^{16}R^{17}$, -$(CH_2)_sSO_2R^{16}$, -$(CH_2)_sSO_2NR^{16}R^{17}$ and -$(CH_2)_sNHSO_2R^{16}$;

R^{16} is selected from hydrogen, C_{1-6}alkyl optionally substituted by up to two hydroxy groups, -$(CH_2)_tOR^{18}$, -$(CH_2)_tNR^{18}R^{19}$, -$(CH_2)_tNHSO_2R^{18}$, -$(CH_2)_tCONR^{18}R^{19}$, -$(CH_2)_tCOOR^{18}$, -$(CH_2)_t$heteroaryl optionally substituted by up to two groups independently selected from halogen, C_{1-6}alkyl and oxo, and -$(CH_2)_t$phenyl optionally substituted by up to two groups independently selected from halogen, C_{1-6}alkyl and C_{1-6}alkoxy,

R^{17} is selected from hydrogen and C_{1-6}alkyl, or

R^{16} and R^{17}, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15}, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen and C_{1-6}alkyl;

R^{18} and R^{19} are each independently selected from hydrogen and C_{1-6}alkyl optionally substitued by up to two hydroxy groups, or

R^{18} and R^{19}, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15}, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen and C_{1-6}alkyl;

m is selected from 0, 1, 2, 3 and 4, wherein each carbon atom of the resulting carbon chain may be optionally substituted with up to two groups independently selected from C_{1-6}alkyl and halogen;

n is 1;
p is selected from 0, 1 and 2;
q is selected from 0, 1, 2 and 3;
r is selected from 0 and 1;
s is selected from 0, 1, 2, 3 and 4; and
t is selected from 1, 2, 3 and 4;
or a pharmaceutically acceptable derivative thereof.

2. A compound according to claim 1 wherein R^1 is selected from C_{1-6}alkyl, C_{3-7}cycloalkyl and phenyl optionally substituted by up to three groups selected from R^5 and R^6.

3. A compound according to claim 1 or claim 2 wherein R^1 is C_{3-6}cycloalkyl.

4. A compound according to any one of the preceding claims wherein R^2 is hydrogen.

5. A compound according to any one of the preceding claims wherein m is 0 or 1.

6. A compound according to any one of the preceding claims wherein m is 1.

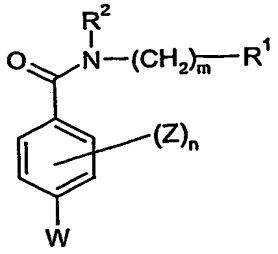
7. A compound according to any one of the preceding claims wherein R^8 is C_{3-6}cycloalkyl.

8. A compound according to any one of the preceding claims wherein Z is selected from $-(CH_2)_sOR^{16}$, $-(CH_2)_sNR^{16}R^{17}$, $-(CH_2)_sNHCOR^{16}$, $-(CH_2)_sNHCONR^{16}R^{17}$ and $-(CH_2)_sNHSO_2R^{16}$.

9. A compound according to claim 1 substantially as hereinbefore defined with reference to any one of Examples 1 to 48, or a pharmaceutically acceptable derivative thereof.

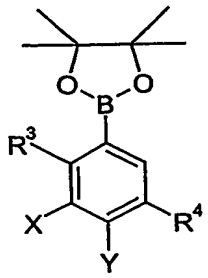
10. A process for preparing a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable derivative thereof, which comprises:

(a) reacting a compound of (II)



(II)

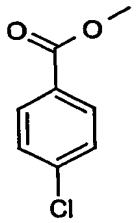
in which R^1, R^2, Z, m and n are as defined in claim 1 and W is halogen, with a compound of formula (III)



(III)

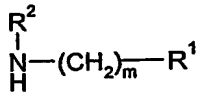
in which R^3, R^4, X and Y are as defined in claim 1, in the presence of a catalyst, or

(b) reacting a compound of formula (VIII)



(VIII)

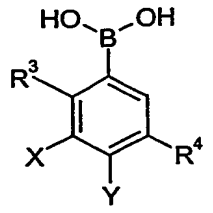
with a compound of formula (III) as hereinbefore defined and then reacting the acid thus formed with an amine of formula (V)



(V)

in which R^1, R^2 and m are as defined in claim 1, under amide forming conditions

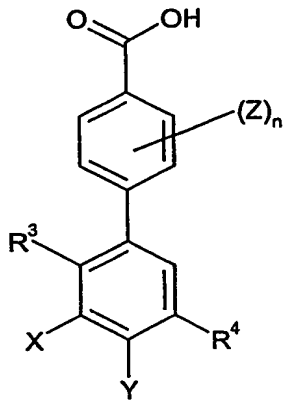
(c) reacting a compound of formula (II) as hereinbefore defined with a compound of formula (IX)



(IX)

in which R^3, R^4, X and Y are as defined in claim 1,
in the presence of a catalyst,

(d) reacting a compound of formula (X)

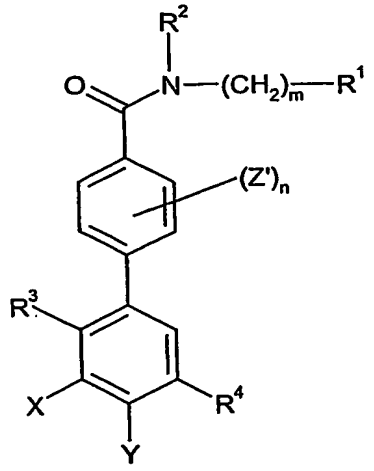


(X)

in which R^3, R^4, X, Y, Z and n are as defined in claim 1,
with an amine compound of formula (V) as defined above,
under amide forming conditions,

(e) final stage modification of one compound of formula (I) into another compound of formula (I), or

(f) conversion of a compound of formula (XII)



(XII)

in which Z' is a group convertible to Z as defined in claim 1.

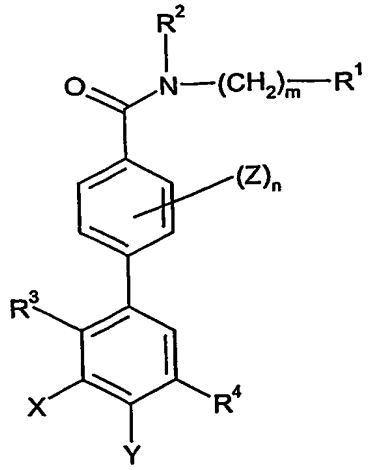
11. A pharmaceutical composition comprising at least one compound according to any one of claims 1 to 9, or a pharmaceutically derivative thereof, in association with one or more pharmaceutically acceptable excipients, diluents and/or carriers

12. A method for treating a condition or disease state mediated by p38 kinase activity or mediated by cytokines produced by the activity of p38 kinase comprising administering to a patient in need thereof a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable derivative thereof.

13. A compound according to any one of claims 1 to 9, or a pharmaceutically acceptable derivative thereof, for use in therapy.

14. Use of a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable derivative thereof, in the manufacture of a medicament for use in the treatment of a condition or disease state mediated by p38 kinase activity or mediated by cytokines produced by the activity of p38 kinase.

15. A compound of formula (IA):



(IA)

wherein

R^1 is selected from hydrogen, C_{1-6}alkyl optionally substituted by up to three groups independently selected from C_{1-6}alkoxy, halogen and hydroxy, C_{2-6}alkenyl, C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, phenyl optionally substituted by up to three groups independently selected from R^5 and R^6, and heteroaryl optionally substituted by up to three groups independently selected from R^5 and R^6,

R^2 is selected from hydrogen, C_{1-6}alkyl and -$(CH_2)_p$-C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups,

or $(CH_2)_mR^1$ and R^2, together with the nitrogen atom to which they are bound, form a four- to six-membered heterocyclic ring optionally substituted by up to three C_{1-6}alkyl groups;

R^3 is chloro or methyl;

R^4 is the group -NH-CO-R^7 or -CO-NH-$(CH_2)_p$-R^8;

R^5 is selected from C_{1-6}alkyl, C_{1-6}alkoxy, -$(CH_2)_p$-C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, -$CONR^9R^{10}$, -$NHCOR^{10}$, -SO_2NHR^9, -$(CH_2)_qNHSO_2R^{10}$, halogen, CN, OH, -$(CH_2)_qNR^{11}R^{12}$, and trifluoromethyl;

R^6 is selected from C_{1-6}alkyl, C_{1-6}alkoxy, halogen, trifluoromethyl and -$(CH_2)_qNR^{11}R^{12}$;

R^7 is selected from hydrogen, C_{1-6}alkyl, -$(CH_2)_p$-C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, trifluoromethyl, -$(CH_2)_r$heteroaryl optionally substituted by R^{13} and/or R^{14}, and -$(CH_2)_r$phenyl optionally substituted by R^{13} and/or R^{14};

R^8 is selected from hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, $CONHR^9$, phenyl optionally substituted by R^{13} and/or R^{14}, and heteroaryl optionally substituted by R^{13} and/or R^{14};

R^9 and R^{10} are each independently selected from hydrogen and C_{1-6}alkyl, or

R^9 and R^{10}, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom

selected from oxygen, sulfur and N-R^{15}, wherein the ring is optionally substituted by up to two C_{1-6}alkyl groups;

R^{11} is selected from hydrogen, C_{1-6}alkyl and -$(CH_2)_p$-C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups,

R^{12} is selected from hydrogen and C_{1-6}alkyl, or

R^{11} and R^{12}, together with the nitrogen atom to which they are bound, form a five or six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15};

R^{13} is selected from C_{1-6}alkyl, C_{1-6}alkoxy, -$(CH_2)_p$-C_{3-7}cycloalkyl optionally substituted by one or more C_{1-6}alkyl groups, -$CONR^9R^{10}$, -$NHCOR^{10}$, halogen, CN, -$(CH_2)_qNR^{11}R^{12}$, trifluoromethyl, phenyl optionally substituted by one or more R^{14} groups and heteroaryl optionally substituted by one or more R^{14} groups;

R^{14} is selected from C_{1-6}alkyl, C_{1-6}alkoxy, halogen, trifluoromethyl and -$NR^{11}R^{12}$;

R^{15} is selected from hydrogen and methyl;

X and Y are each independently selected from hydrogen, methyl and halogen;

Z is selected from -$(CH_2)_sOR^{16}$, -$(CH_2)_sNR^{16}R^{17}$, -$(CH_2)_sCH_2CH_2R^{16}$, -$(CH_2)_sCOOR^{16}$, -$(CH_2)_sCONR^{16}R^{17}$, -$(CH_2)_sNHCOR^{16}$, -$(CH_2)_sNHCONR^{16}R^{17}$, -$(CH_2)_sSO_2R^{16}$, -$(CH_2)_sSO_2NR^{16}R^{17}$ and -$(CH_2)_sNHSO_2R^{16}$;

R^{16} is selected from hydrogen, C_{1-6}alkyl, -$(CH_2)_tOR^{18}$, -$(CH_2)_tNR^{18}R^{19}$, -$(CH_2)_tCOOR^{18}$, -$(CH_2)_t$heteroaryl optionally substituted by up to two groups independently selected from halogen and C_{1-6}alkyl, and -$(CH_2)_t$phenyl optionally substituted by up to two groups independently selected from halogen, C_{1-6}alkyl and C_{1-6}alkoxy,

R^{17} is selected from hydrogen and C_{1-6}alkyl, or

R^{16} and R^{17}, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15}, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen and C_{1-6}alkyl;

R^{18} and R^{19} are each independently selected from hydrogen and C_{1-6}alkyl, or

R^{18} and R^{19}, together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R^{15}, wherein the ring is optionally substituted by up to two groups independently selected from oxo, halogen and C_{1-6}alkyl;

m is selected from 0, 1, 2, 3 and 4, wherein each carbon atom of the resulting carbon chain may be optionally substituted with up to two groups independently selected from C_{1-6}alkyl and halogen;

n is 1;

p is selected from 0, 1 and 2;

q is selected from 0, 1, 2 and 3;

r is selected from 0 and 1;

s is selected from 0, 1, 2, 3 and 4; and

t is selected from 2, 3 and 4;

or a pharmaceutically acceptable derivative thereof.